REMARKS

The attached pages include no new matter and are part of the original disclosure under 37 CFR §1.53(d)(2), but do not yet appear to have been made of record in the subject application.

CONCLUSION

In view of the foregoing, Applicants believe this application to be in condition for substantive review on the merits.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 925-472-5000.

Respectfully submitted,

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Attachments
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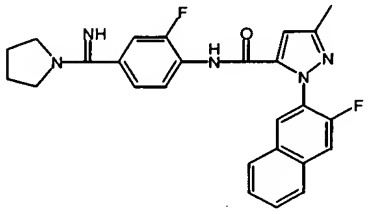
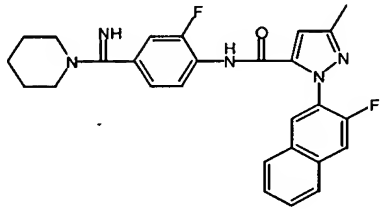
to dryness. The solid was dissolved in 5 mL dry methanol. To it was added anhydrous N-methylethylenediamine (0.5 mL). The mixture was refluxed for 1 hour, concentrated and loaded on prep HPLC to afford the title compound in 80% yield. ES-MS: $(M+H)^+$ 446.

Example 23



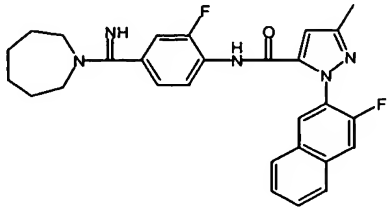
This compound was prepared by the same methodology described for Example 22 with pyrrolidine substituted for N-methylethylenediamine. ES-MS: $(M+H)^+$ 460.

Example 24.



This compound was prepared by the same methodology described for Example 22 with piperidine substituted for N-methylethylenediamine. ES-MS: $(M+H)^+$ 474.

Example 25.

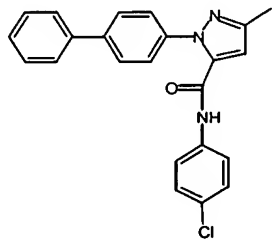


and washed with brine (X2). The organic phase was dried, concentrated and subjected on flash column to isolate ethyl 3-methyl-1-(5-N-tert-butylaminocarbonyl-2-methylsulfonylphenyl)-1H-pyrazole-5-carboxylate (0.74 g, 30%). Rf 0.70 (pure EtOAc). ES-MS: $(M+H)^+$ 408.

Step 5. To a solution of 2'-N-tert-butylaminosulfonyl-[1,1']-biphenyl-4-ylamine (100 mg, 0.33 mmol) in 2 mL DCM was added trimethylaluminum (2.0M in hexane, 0.66 mL, 1.3 mmol) under argon at room temperature. After being stirred for 30 minutes, to the mixture was added the above-prepared ester (90 mg, 0.22 mmol) in 10 mL DCM. The resulting mixture was stirred overnight. The reaction was quenched using 10 mL saturated Rochelle's salt aq solution. The mixture was extracted using DCM (X3). The organic phases were combined, dried, rotovaped and subjected on flash chromatography column to give the coupled product in 62% yield (90 mg). Rf 0.10 (1:1 EtOAc: hexane). ES-MS: $(M+H)^+$ 666.

Step 6. The above-prepared compound (20 mg) was placed in 5 mL TFA. It was stirred at 70°C for 1 hour and subjected on prep HPLC to isolate the title compound (90%) after evaporation. ES-MS: $(M+H)^+$ 554.

Example 129.

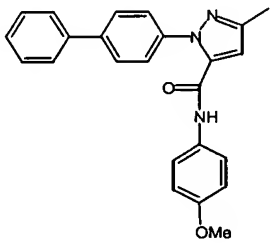


Step 1. To a solution of 4-biphenylboronic acid (1.0 g, 5.1 mmol) and ethyl 3-methylpyrazole-5-carboxylate (0.78 g, 5.1 mmol) in 25 mL dry DCM were added pyridine (1.2 mL, 15 mmol) and anhydrous powder of copper(II) acetate (1.84 g, 10 mmol). Some activated molecular sieve powder was added afterwards. The resulting

slurry was refluxed for 2 days under argon. The mixture was diluted with DCM, filtered through celite. The blue filtrate was washed with water (X2), dried, concentrated, purified with flush column to yield ethyl 3-methyl-1-(4-phenylphenyl)-1H-pyrazole-5-carboxylate (26%), Rf 0.67 (1:2 EtOAc: hexane), ES-MS: $(M+H)^+$ 307; and its regioisomer, ethyl 5-methyl-1-(4-phenylphenyl)-1H-pyrazole-3-carboxylate (31%), Rf 0.50 (1:2 EtOAc: hexane), ES-MS: $(M+H)^+$ 307.

Step 2. To a stirred solution of 4-chloroaniline (24 mg, 0.18 mmol) in 1 mL DCM was added trimethylaluminum (2.0M, 0.43 mL, 0.86 mmol) at room temperature. After 30 minutes, to the mixture was added ethyl 3-methyl-1-(4-phenylphenyl)-1H-pyrazole-5-carboxylate (52 mg, 0.17 mmol) in 3 mL DCM. The resulting mixture was stirred for overnight. It was quenched using 5 mL saturated Rochelle's salt aq solution. The mixture was extracted using DCM (X3). The organic phases were combined, dried, concentrated and subjected on flash column to afford the title compound (46 mg, 70%). Rf 0.46 (1:1 EtOAc: hexane). ES-MS: $(M+H)^+$ 388.

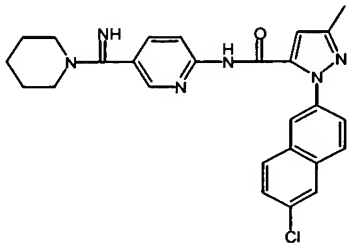
Example 130.



The title compound was prepared using the same methodology shown for Example 129, with 4-methoxyaniline substituted for 4-chloroaniline. ES-MS: $(M+H)^+$ 384.

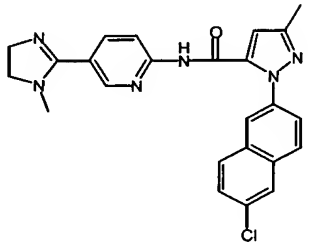
The title compound was prepared using the same methodology shown for Example 119, with 2-amino-5-cyanopyridine substituted for 4-amino-3-fluorobenzonitrile. ES-MS: $(M+H)^+$ 459.

Example 199.



The title compound was prepared using the same methodology shown for Example 120, with 2-amino-5-cyanopyridine substituted for 4-amino-3-fluorobenzonitrile. ES-MS: $(M+H)^+$ 473.

Example 200.

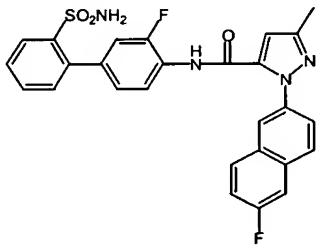


The title compound was prepared using the same methodology shown for Example 118, with 2-amino-5-cyanopyridine substituted for 4-amino-3-fluorobenzonitrile. ES-MS: $(M+H)^+$ 445.

The residue was taken into chloroform, washed with water, dried, concentrated in vacuuo to give 6-fluoro-2-naphthylamine (50%). Rf 0.53 (1:1 EtOAc: hexane). ES-MS: $(M+H)^+$ 162.

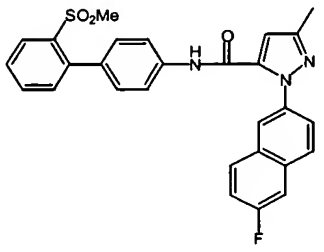
Step 4. The title compound was prepared using the same methodology shown for Example 115, with 6-fluoro-2-naphthylamine substituted for 6-chloro-2-naphthylamine. ES-MS: $(M+H)^+$ 501.

Example 219.



The title compound was prepared using the same methodology shown for Example 218, with 2'-N-tert-butylaminosulfonyl-3-fluoro-[1,1']-biphenyl-4-ylamine substituted for 2'-N-tert-butylaminosulfonyl- [1,1']-biphenyl-4-ylamine. ES-MS: $(M+H)^+$ 519.

Example 220.



The title compound was prepared using the same methodology shown for Example 218, with 2'-methylsulfonyl-[1,1']-biphenyl-4-ylamine substituted for 2'-N-tert-butylaminosulfonyl-[1,1']-biphenyl-4-ylamine. ES-MS: $(M+H)^+$ 500.